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Formulation and Evaluation of Carvedilol Oral Disintegrating Tablets

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A B S T R A C T

The oral medication is easy to manufacture, compact, and convenient for self-administration, it is regarded as the most frequently approved method of administration. Due to their substantial influence on patient compliance, oral disintegrating tablets (ODT) have become more popular. New ODT technologies enable high drug loading, palatable taste, pleasant mouth feel, and minimal mouth residue following oral administration. ODT have been investigated for their potential in improving bioavailability of poorly soluble drug through enhancing the dissolution profile of the drug and hepatic metabolism drugs. The goal of the current study was to design and assess carvedilol fast-dissolving tablets for the efficient treatment of angina pectoris, hypertension, and other conditions. Considering its shorter plasma half-life and significant first pass effect. This study was attempted to create and assessed Carvedilol oral disintegration tablets using the direct compression method by using a variety of super disintegrants like cross povidone (XL-PVP), Croscarmellose sodium (Ac-Di-Sol®) sodium starch glycolate along with other excipients and 9 formulations were prepared. The formulations were subjected for both the evaluation of pre and post formulation studies. DSC and IR spectroscopy data shown the characterization of drug, excipient, compatibility of drug and solid dispersion with excipients, gave evidence of solid dispersion formation and UV absorption spectra shown enhancement of solubility. Various preformulation batches (F1- F9) formulated by direct compression method using different concentrations of polymers. After a number of evaluation processes, it was found that F9 formulation met all requirements for the fast oral disintegration tablets by using Carvedilol with cross povidone and drug release was found to be 98.97%.

Keywords: Carvedilol, Disintegration, Cross Povidone, Sodium Starch Glycolate.

A R T I C L E I N F O

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C O N T E N T S

1. Introduction

The oral route of administration is considered as the most widely accepted route because of its convenience of self-administration, compactness and easy manufacturing[1-4]. However, the most obvious disadvantage of the widely used oral dosage forms, such as tablets and capsules, is that they are difficult for patients to swallow, which can make them noncompliant, especially in the case of paediatric and geriatric patients[5-9]. This also applies to individuals who are sick in bed, as well as patients who are busy or on the go, especially those without access to water[10-14].Since it significantly affects patient compliance, the need for the creation of fast-disintegrating tablets, or FDTs, has expanded dramatically during the past ten years[15-20]. A sizable portion of the populace enjoys fast-disintegrating pills, especially those who have swallowing issues[21-24]. According to reports, dysphagia, or trouble swallowing, affects people of all ages but is more prevalent in the juvenile and geriatric populations as well as in

institutionalized and psychiatric settings, as well as in patients who have difficulties from motion sickness, nausea, and vomiting. FDTs with pleasing flavours and tastes help different demographic groups absorb bitter medications[25,24]. The benefits of both the liquid and dry formulations are combined in this dose form[26]. High drug loading, a tolerable taste, a pleasing mouthfeel, and little to no residue in the mouth following oral delivery are all made possible by some innovative FDT technologies[27-29]. FDT has been studied for its potential to increase the hepatic metabolism of pharmaceuticals and the bioavailability of poorly soluble medications by modifying the drug's solubility profile[30]. The terms dispersible tablets, mouth dissolving tablets, fast disintegrating tablets, fast dissolving tablets, rapid-dissolving tablets, and porous tablets are other names for fast disintegrating pills[31,32].

Carvedilol

IUPAC Name: 1-(9H-carbazol-4-yloxy)-3-{[2-(2-methoxy phenoxy) ethyl]amino}propan-2-ol

Chemical Formula: C24H26N2O4[33].

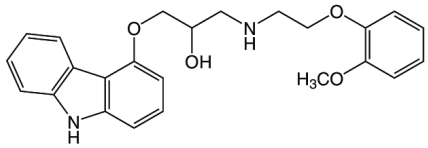

Figure:1 Structure of Carvedilol

2. Materials and methods

The formulation and assessment investigations made use of the drug material, resin, excipients, and chemicals. Carvedilol was gift sample of Ajanta Pharma Ltd, Mumbai, and Maharashtra. Cross Povidone, Sodium starch glycolate and Croscarmellose sodium (Ac-Di-Sol®) were procured from Research-lab fine chem. Industries, Mumbai. All other chemicals were of analytical grade and were used without further purification.

Technology Used for Manufacturing of Orally Disintegrating Tablets

Direct compression is the simplest method of producing tablets. This method was shown to be better due to its low manufacturing costs, use of common equipment, and minimal processing stages. Disintegrating, water-soluble excipients, and effervescing agents can act alone or in combination to cause the disintegration and dissolving of directly compressed tablets. To guarantee rapid disintegration and dissolution, it is crucial to select an appropriate and ideal disintegrant concentration. Super disintegrants are more recent compounds with higher mechanical strength and disintegration efficiency that work better at lower concentrations. The super disintegrants undergo a disruptive change in the tablet upon coming into contact with water. They hydrate, swell, and alter in volume or form. Super disintegrants that are effective offer enhanced compressibility, compatibility, and do not adversely affect the mechanical strength of formulations that contain high dosage medications.

The kind of disintegrants and their ratio are crucial factors. Particle size distribution, contact angle, pore size distribution, and water absorption capacity are other variables to be taken into account. Research findings indicate that super disintegrants that are insoluble in water, such as sodium starch glycolate and croscarmellose sodium, exhibit superior disintegration properties compared to agents that are slightly soluble in water, such as cross povidone, due to their lack of swelling tendency. Super disintegrants with a tendency to swell exhibit a slight disintegration property retardation as a result of the viscous barrier forming. The amount of super disintegrant can be as high as necessary as long as the tablet's mechanical characteristics allow it to be used for the intended purpose. It is possible to employ the super disintegrant by itself or in conjunction with other super disintegrants.

Formulation

Preparation of the Fast disintegrating tablet of Carvedilol: Prepare tablet by direct compression method using the 10-station rotary punch tablet compression machine using 7 mm biconvex plain on both side die-punches set. The drug Carvedilol and super disintegrant like cross povidone, Mannitol (diluent), Magnesium stearate (lubricant), Talk (glidant), Microcrystalline cellulose (Binder), Aspartame (sweetener), Strawberry (flavour). Weigh all ingredient and passed through mesh no. 60 excepting lubricants. Lubricants were passed through mesh no.80. Lubricants were added at the time of compression. The blend is mixed uniformly by manually for 30 minutes.

3. Results and Discussion

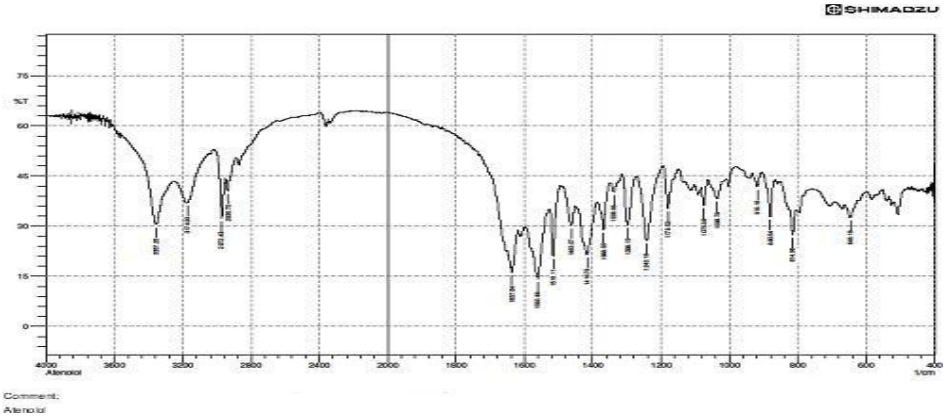

Figure:2 FT-IR Spectrum of Carvedilol

Table :2 Functional group analysis of Carvedilol

S.No	Peaks	Functional group
1	3668.62&3346.30	OH (Alcohol)
2	3051.96	Aromatic C-H Stretching
3	3015.42	Alkene C-H Stretching
4	2950.80&2893.72	Alkane C-H Stretching
5	1730.91&1709.46	Ketone
6	1621.74	NH(Amine)
7	1396.31,1372.09,1351.93& 1325.98	C-O(Phenol)
8	1081.22,1159.04,1182.78	C-N Vibrations
9	600-900	C-H Bending (Aromatic)

C. Calibration curve Carvedilol

Calibration of Carvedilol by UV- spectrophotometer method, revealed a $\lambda_{max}$of 226 nm. The standard calibration curve was constructed from concentrations range 2 -12µg/mL,byusingpH6.8phosphatebufferinsaliva.The correlation coefficient (R^2) was found to be 0.999.

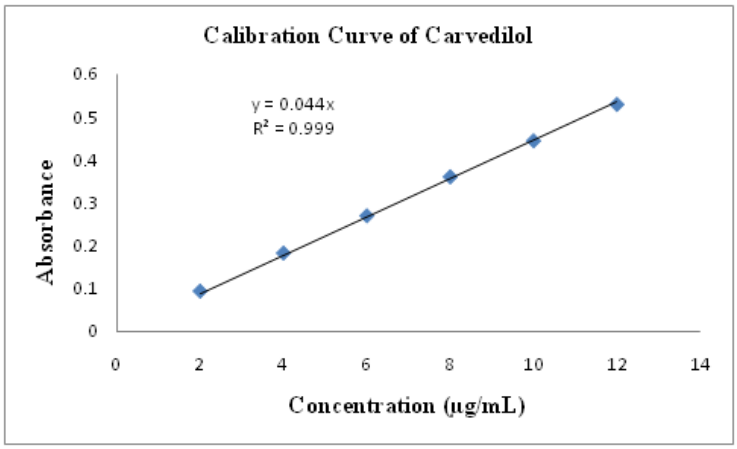

Figure : 3 Standard Calibration curve of Carvedilol

Table : 3 Evaluation parameters of tablets

Formulation Code	Weight Variation (mg)	Friability (%)	Hardness (Kg/cm2)	Thickness (mm)
F1	176.1±1.21	0.396	3.83±0.28	2.95±0.05
F2	176.1±1.33	0.524	3.16±0.28	2.91±0.05
F3	175.3±1.02	0.402	3.66±0.28	2.95±0.04
F4	176.5±1.01	0.530	3.83±0.28	2.91±0.06
F5	176.25±0.37	0.658	3.33±0.28	2.86±0.05
F6	175.9±1.65	0.663	3.16±0.28	2.88±0.03
F7	177±1.85	0.796	3.50±0.50	2.83±0.04
F8	175.1±0.70	0.671	3.16±0.28	2.85±0.07
F9	176.5±0.76	0.656	3.16±0.76	2.83±0.04

Table:4 Drug Content evaluation parameters of tablets

Formulation Code	Diameter (mm)	Disintegration (Sec)	Wetting Time (sec)	Drug Content (%)
F1	7.98±0.01	183.66±0.51	98±1.21	100.88±0.88
F2	7.99±0.01	65.66±0.51	66±1.73	98.72±0.44±
F3	7.98±0.01	57.66±1.08	54±1.64	98.52±1.17
F4	7.99±0.02	48.33±0.51	38±1.10	98.82±1.83
F5	7.99±0.05	35.66±1.08	30±0.64	97.41±1.63
F6	7.99±0.02	29.33±1.08	28±0.64	101.17±1.78
F7	7.99±0.01	33.66±1.52	29±0.64	97.11±1.28
F8	7.97±0.03	28±1.00	27.6±0.57	97.99±1.98
F9	8.00±0.05	18.33±1.15	18±0.64	98.92±0.78

Table: 5 *In-vitro* release of Carvedilol from formulation sF1-F9

Time (min)	**%Cumulative Drug Release**								
	F1	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**
0	0	0	0	0	0	0	0	0	0
0.5	16.56	17.28	18.54	26.92	29.32	33.41	28.57	46.32	49.32
1	22.98	23.42	25.46	33.76	37.43	39.97	34.56	51.42	54.62
1.5	31.42	33.76	34.92	42.26	46.52	48.87	43.72	58.92	61.92
2	39.54	41.96	43.56	49.56	53.25	55.72	51.76	64.56	66.57
2.5	46.76	47.84	49.76	52.34	57.26	59.47	53.42	70.52	71.14
3	52.78	54.72	55.42	58.64	63.45	65.42	59.76	74.97	76.52
3.5	59.92	61.11	63.76	64.72	69.42	71.92	66.11	79.68	82.49
4	62.54	64.92	66.98	68.23	76.83	78.47	72.59	84.65	88.56
4.5	71.36	72.58	73.51	74.76	82.65	86.97	83.92	89.34	91.72
5	79.42	80.56	81.96	81.43	89.54	92.51	91.42	92.37	98.97

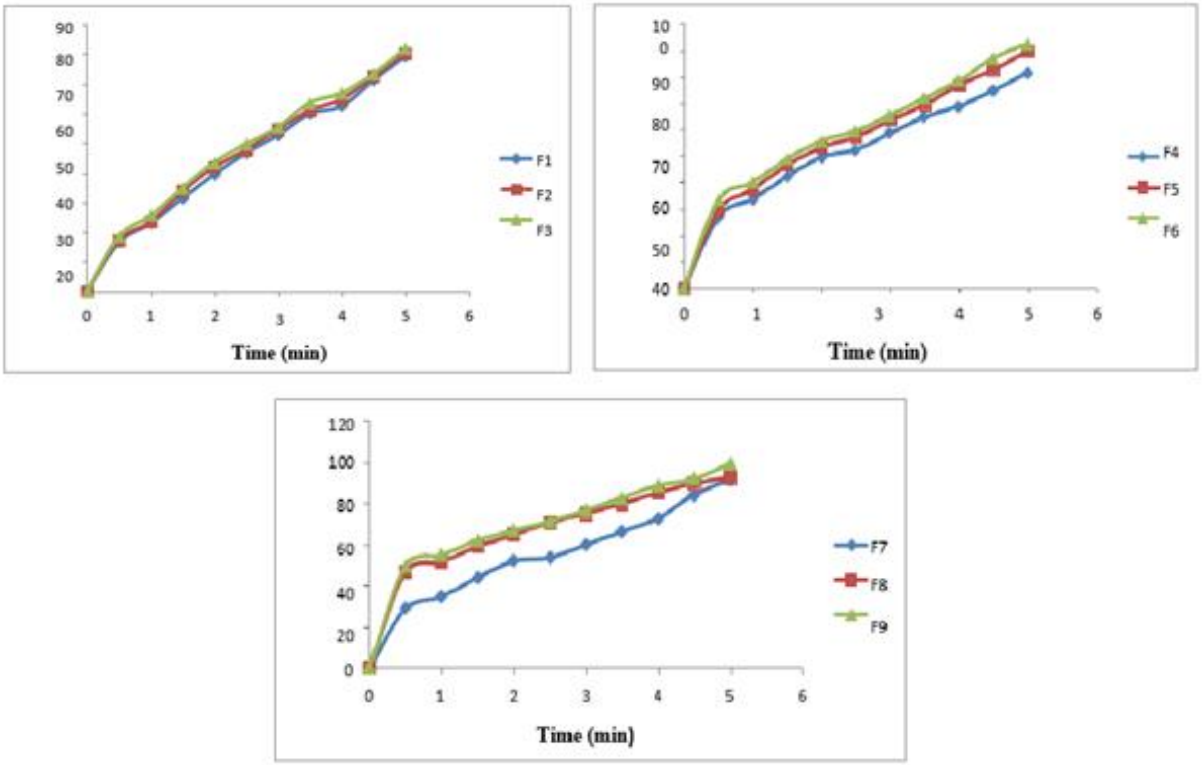

Figure : 4 Comparative dissolution of Carvedilol for formulations (F1-F9)

In-vitro dissolution study:

In-vitro dissolution studies were performed in pH6.8 phosphate buffer. From the above data it is evident that the promising formulation 9 released 98.97% drug in 5 minutes (pH 6.8 phosphate buffer).This study attempted to created and assessed Carvedilol Oral Dispersible Tablets by direct compression method, using a variety of Super disintegrants like Cross povidone (XL-PVP), Croscarmellose sodium (Ac-Di-Sol®), Sodium starchglycolate are along with other excipients 9 formulations are prepared. The formulations were subjected for both the evaluation of pre and post formulation studies. Hardness and friability: It was discovered that the tablet formulations hardness ranged from 3.16 to 3.83kg/cm 2. It was discovered that the friability values ranged from 0.30 to 0.6%. Disintegration time: The disintegration time of formulation 9th was 18sec which is the best result obtained than the rest of the formulation. Uniformity of weight: All the prepared tablets of Carvedilol were evaluated for weight variation. The weigh to fall the tablets was found to be uniform with low values of standard deviation and within the prescribed IP limits of ±5%. Uniformity of drug content: The low values of standard deviation indicate uniform drug content with in the tablets. It was discovered that the drug content of each table arranged from 97.11% to 100.88%.

4. Conclusion

Oral Dispersible Tablets of Carvedilol were formulated and evaluated with the objective of providing rapid onset of action in the treatment of Hypertension. After a number of evaluation processes, it was found that F9 met all the requirements for the Oral dispersible tablets. In-vitro release studies were carried out for all formulations to quantify percentage cumulative release of drug. Based on

the drug release profile suitable formulation was selected. The formulation F9 was shown 98.97% of drug release when compared to other formulations. In this research Korsmeyer-Peppas is the best fitting model that explains the drug release mechanism of the dispersible tablets. The n value obtained in the Korsmeyer-Peppas equation is less than 1 for all the formulations indicating that the drug release follows non-Fickian diffusion. Henceit maybe concluded that formulation of oral dispersible tablets surely enhances the patient compliance by producing rapid onset of with minimum dose and further studies have to be carried out in future to develop a new dosage form of Carvedilol to satisfy the need of patients.

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